Claims 3, 4, and 7-14 are presented for examination at this time.

35 U.S.C. § 103

35 U.S.C. § 103 over Rowinsky et al., Holmes et al. and Gilman et al.

Claims 1 and 3-11 have been rejected under 35 U.S.C. § 103 as allegedly being unpatentable over Rowinsky et al., Holmes et al., and Gilman et al. of record.

Applicants traverse the rejection.

It is respectfully submitted that although Gilman et al. is stated to be of record by the Examiner, applicants find no evidence of the citation of this reference in the record of the subject application. It is respectfully requested that the complete citation of the Gilman et al. reference and the teachings therein be provided to applicants.

Notwithstanding, the Examiner alleges that the Rowinsky et al. reference teaches the applicants' taxol [treatment] for 24 hours at 200-250 mg/m^2 by i.v. infusion; that the Holmes et al. reference teaches taxol for treating breast cancer at 250 mg/m^2 for 24 hours of infusion every 21 days; and that the Gilman et al. reference teaches 30 mg/m^2 per day for 5 days or 210 mg - 250 mg given every three weeks. The Examiner alleges that the difference among these is in the number of hours and the amount being employed and that in view of this, "one skilled in the art could be motivated to employ the i.v. infusion of the prior art for a long period of time in the absence of a side-by-side comparison.".

It is submitted that the existence of various taxol dosing schedules and regimens for treatment of different cancers or blood diseases does not *a priori* make one schedule obvious over another. The distinct and nonobvious differences among drug and treatment regimens was explained and discussed at length in applicants' amendment filed on November 8, 1993. Further and importantly, the prior art teaches away from the

instant invention as claimed, since the art recommends and uses greater quantities of taxol for shorter administration times. It is submitted that the length of time that a given amount of a drug (e.g., taxol as described herein) is provided to a patient can make a significant difference in the response of the patient to the drug and in the drug's effectiveness in combatting and/or overcoming disease. In this regard, a drug dosing regimen, in particular, a taxol dosing regimen, and its effectiveness, or lack thereof, can be neither predicted nor obvious, because the regimen must be tested and the results assessed, preferably in a randomized and blind study. It is also submitted that most trials involving dosing schedules are "hit or miss" processes, with doses and administration times determined empirically by particular physicians, clinicians, or groups thereof; the predictability of the outcome is unreasonable in the absence of a trial or experimental protocol using a given dosing schedule to determine the outcome. This points further to the nonobviousness of the present invention in view of the cited art.

In addition, a Declaration of Dr. Wyndham H. Wilson under 37 C.F.R. § 1.132 is to be timely submitted subsequent to the filing of this amendment to verify the nonobviousness of the claimed invention and to demonstrate that the taxol dosing schedule in accordance with the instant invention showed superior results compared with a study in which a higher dose of taxol was used in a 24 hour treatment schedule to treat patients with refractory breast cancer.

It is respectfully asserted that the studies of Rowinsky et al., Holmes et al., and (allegedly) Gilman et al. all teach different taxol dosing schedules, and use higher amounts of taxol over differing time periods, notably 24 hours. Both Rowinsky et al. and Holmes et al. teach different taxol dosing regimens (higher dose, shorter time period) for various indications and report varying results. While Rowinsky et al. teach taxol doses of between 200-390 mg/m^2 over 24 hours, Holmes et al. teach taxol given

at a dose of 250 mg/m² over 24 hours. These teachings are distinct from the present invention as claimed and do not suggest or make obvious the applicants' inventive discovery as claimed.

In view of the remarks presented above and the Declaration of Dr. W. Wilson, it is respectfully requested that the rejection of the claims under 35 U.S.C. § 103 be withdrawn.

35 U.S.C. § 112, second paragraph

Claims 1 and 3-11 have been rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. Applicants traverse the rejection and believe that the cancellation of claims 1, 5, and 6 and the replacement of these cancelled claims with new claims 12, 13, and 14, respectively, alleviates the rejection of the base claims. The amendments to the claims as presented herein are believed to overcome the examiner's rejection under 35 U.S.C. § 112, second paragraph. Accordingly, withdrawal of the rejection is respectfully requested.

CONCLUSION

Based upon the foregoing, Applicants respectfully believe that the subject matter of the claims is free of the prior art and that the application and claims are now in condition for allowance. An action passing this case to issue is courteously urged.

Respectfully submitted,

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